Hemoglobinopathy Fact Sheet

Hemoglobin Bart's

Hemoglobin Bart's is a relatively common hemoglobin variant that is seen only during the newborn period. The presence of hemoglobin Bart's almost always indicates that one or more of the baby's four genes that produce alpha globin chains is dysfunctional, causing alpha thalassemia. The level of Bart's (low, moderate or high) usually correlates with the number of alpha genes affected. The more alpha genes affected, the more significant the thalassemia and clinical symptoms. Alpha thalassemia occurs in individuals of all ethnic backgrounds and is one of the most common genetic diseases worldwide. However, the clinically significant forms (Hemoglobin H disease and Fetal Hydrops Syndrome) occur predominantly among Southeast Asians. Summarized below are the manifestations of different numbers of affected genes and recommendations for follow-up of Hemoglobin Bart's. Genetic counseling is advisable for families affected by these conditions to promote understanding of the significance for them and future offspring.

ONE dysfunctional alpha gene: **Silent Carrier**
If one alpha gene is affected, the other three genes can compensate nearly completely. These individuals are clinically and hematologically normal. (Follow-up is for the benefit of determining reproductive risks for the family.)

TWO dysfunctional genes: **Alpha Thalassemia Trait**
Dysfunction of two alpha genes results in a mild anemia with microcytosis. This is benign and requires no treatment. (Follow-up is for the benefit of determining reproductive risks for the family, which will differ depending on whether the two dysfunctional genes are on the same or different chromosomes.)

THREE dysfunctional genes: **Hemoglobin H Disease**
Three dysfunctional alpha genes generally results in a moderate hemolytic anemia. Family studies usually demonstrate that one parent is a silent carrier (one dysfunctional alpha gene) and the other has alpha thalassemia trait (two dysfunctional alpha genes). The clinical manifestations of this disorder are variable but most patients are anemic and develop some degree of splenomegaly. Hemoglobin H is unstable and patients with hemoglobin H disease have chronic hemolysis in addition to alpha thalassemia. They are susceptible to accelerated hemolysis when exposed to the same drugs that cause hemolysis in subjects with glucose-6-phosphate dehydrogenase (G6PD) deficiency. A list of these drugs can be furnished on request.

FOUR (all) genes dysfunctional: **Fetal Hydrops Syndrome**
If none of the alpha genes are functional, a very severe hemolytic anemia begins in utero. The anemia is so severe that the disorder is lethal with fetal demise usually occurring in the third trimester. Also, pregnant women carrying an infant with fetal hydrops syndrome have a high rate of severe toxemia of pregnancy. Family studies usually reveal that both parents have alpha thalassemia trait (two alpha gene deletions). Prospective parent screening and intrauterine diagnosis are appropriate if the potential for fetal hydrops syndrome is suspected.

Follow-up of Newborns with Hemoglobin Bart's

At Two to Three Months

Examine baby for splenomegaly and do a complete blood count (CBC). (Enlargement of the spleen, microcytosis and anemia indicate increased risk of Hemoglobin H disease).

- If both are normal, and no other hemoglobin abnormality other than Hemoglobin Bart's was present at birth, Hemoglobin H disease is unlikely and no further work-up is required until 9 to 12 months.

- If either is abnormal, the infant is at risk of developing Hemoglobin H disease. Consultation with an expert in the assessment of these abnormalities is recommended. The Department of Health can provide a list of physicians and laboratories that can help with this work-up.

The parents of a child with Hemoglobin Bart's who develops microcytosis in infancy should also have a CBC. If either parent is microcytic, further evaluation of the parents for alpha thalassemia is warranted due to the risk of Fetal Hydrops Syndrome in future pregnancies.

Between Nine and Twelve Months

Do a CBC and reticulocytes.

- If normal, the child most likely is a silent carrier and the family is not at risk for Fetal Hydrops Syndrome in future pregnancies. No further work-up is necessary.

- If microcytic, do iron studies:

a) If iron-deficient, treat for 3 to 6 months then repeat the CBC. If microcytosis is corrected, the child most likely is a silent carrier and the family is not at risk for Fetal Hydrops Syndrome in a future pregnancy. No further work-up is necessary.

b) If not iron deficient, (or if microcytosis persists after iron deficiency has been corrected), do a hemoglobin electrophoresis or HPLC (including quantitation of hemoglobins A2 and F). The work-up should include a stain for hemoglobin H inclusion bodies using brilliant cresyl blue. High levels of hemoglobin H inclusion bodies and unresolved microcytic anemia, indicate that the child has Hemoglobin H disease. Lower levels of inclusion bodies are found with alpha thalassemia trait. Consultation with an expert in the assessment of these abnormalities is recommended. The Department of Health can provide a list of physicians and laboratories that can help with this work-up.

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